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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/508,759	09/22/2004	Hyo Jeong Hong	DE1586	9699

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EXAMINER	
BOESEN, AGNIESZKA	

ART UNIT	PAPER NUMBER
1648	

NOTIFICATION DATE	DELIVERY MODE
05/25/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/508,759	HONG ET AL.	
	Examiner	Art Unit	
	AGNIESZKA BOESEN	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-24* is/are pending in the application.

4a) Of the above claim(s) *11-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2 and 3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/4/2010 and 1/20/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to comply*.

DETAILED ACTION

The Amendment filed December 22, 2009 and February 26, 2010 in response to the Office Action of July 21, 2009 is acknowledged and has been entered.

Claims 2, 9 and 10 have been amended. Claims 11-24 are withdrawn. Claims 2-10 are under examination in this Office Action.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 5/4/2010 and 1/20/2010 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Drawings

Applicant's amendment to the drawings to add SEQ ID NO filed February 26, 2010 is acknowledged.

Specification

Applicant's amendment to the specification filed December 22, 2009 is acknowledged.

Sequence Compliance

The sequence listing filed December 22, 2009 is acknowledged. However, it is noted that Applicant must file the sequence listing and the corresponding computer readable form to the address indicated below in order for the sequences to be entered into the database. Thus in order to comply with the sequence rules Applicant must resubmit the sequence listing to the address below:

The addresses below are effective 5 June 2004. Please direct all replies to the United States Patent and Trademark Office via one (1) of the following:

1. Electronically submitted through EFS-Bio

(http://www.uspto.gov/ebc/efs/downloads/documents.htm,

EFS Submission user Manual – ePAVE)

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Claim Rejections - 35 USC § 112

Rejection of claims 6, 7, 9 and 10 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement **is withdrawn** in view of Applicant's amendment to the claims and the drawings.

The Declaration by Attorney of record Eugene Lieberstein filed December 22, 2009 is acknowledged. However the declaration is defective because it does not contain a reference to any specific hybridoma cell lines. Additionally, the declaration does not contain the false willful

statement. Examiner notes however that the Declaration regarding the Biological Deposit is not required to satisfy the enablement requirement because Applicant has provided the SEQ ID NOs representing the antibodies and antibody light and heavy chains recited in the present claims, in the drawing and in the specification as well as the sequence listing, which are sufficient to satisfy the enablement requirement.

Claim Rejections - 35 USC § 103

Rejection of Claim 2 under 35 U.S.C. 103(a) as being obvious over Leong et al. (Cytokine, November 2001, Vol. 16, p. 106-119) **is withdrawn** in view of Applicant's amendment.

Rejection of claim 3 under 35 U.S.C. 103(a) as being obvious over Maeng et al. (Virology, 2000 Vol. 270, p. 9-16) in view of Leong et al. (Cytokine, November 2001, Vol. 16, p. 106-119) **is withdrawn** in view of Applicant's amendment.

New Rejection in view of Applicant's IDS

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kashmiri et al. (Critical Reviews in Oncology/Hematology, 2001, Vol. 38, p. 3-16 in IDS on 1/20/2010) in view of Leong et al. (Cytokine, November 2001, Vol. 16, p. 106-119).

Kashmiri teaches a method of making a humanized antibody consisting of the steps of first performing a mutational analysis to determine the specificity determining residues (SDRs) in the complementarily determining region (CDR) of murine monoclonal antibody CC49 heavy and light chain variable regions, selecting the mutants that have lower affinity to the human antigen than the original murine antibody, determining the replaced amino acid residue of as a specificity determining residue (SDR) and subsequently grafting the SDRs to the corresponding amino acid residues into human antibody variable regions (see pages 5 and 6, Table 1 and Figures 1 and 2).

While Kashmiri teaches mutational analysis of amino acids within the CDRs of the CC49 antibody, Kashmiri does not teach mutations by replacing each amino acid residue with alanine.

Leong et al. teaches a method of making humanized anti-IL-8 antibody comprising performing alanine scanning mutagenesis of the murine CDRs in order to determine the specificity determining residues SDRs (see the entire document, particularly Alanine scanning mutagenesis on page 108, Experimental procedures: Construction of humanized version of anti-IL-8 antibody 6G4.2.5, and Tables 1 and 2).

It would have been *prima facie* obvious to provide Kashmiri's method comprising first performing a mutational analysis to determine the specificity determining residues (SDRs) in the complementarily determining region (CDR) and subsequently grafting the SDR to the corresponding amino acid residues into human antibody variable regions wherein determining the SDRs comprises replacing each amino acid residue of the CDR with alanine as taught by Leong.

One would have been motivated to determine SDRs by doing alanine scanning mutagenesis because Leong teaches that changing each amino acid residue within the CDR to alanine is used to determine which amino acids in the CDR improve or weaken the binding to the antigen (see page 108, left paragraph).

All the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claim 3 is rejected under 35 U.S.C. 103(a) as being obvious over Kashmiri et al. (Critical Reviews in Oncology/Hematology, 2001, Vol. 38, p. 3-16 in IDS on 1/20/2010) in view of Leong et al. (Cytokine, November 2001, Vol. 16, p. 106-119) as applied to claim 2 and further in view of Maeng et al. (Virology, 2000 Vol. 270, p. 9-16 of record on 3/18/2008).

Kashmiri teaches a method of making a humanized antibody consisting of the steps of first performing a mutational analysis to determine the specificity determining residues (SDRs) in the complementarily determining region (CDR) of murine monoclonal antibody CC49 heavy and light chain variable regions, selecting the mutants that have lower affinity to the human antigen than the original murine antibody, determining the replaced amino acid residue of as a

specificity determining residue (SDR) and subsequently grafting said SDR to the corresponding amino acid residues into human antibody variable regions (see pages 5 and 6, Table 1 and Figures 1 and 2).

Leong et al. teaches a method of preparing humanized anti-IL-8 antibody comprising performing alanine scanning mutagenesis of the murine CDRs in order to determine the specificity determining residues SDRs (see the entire document, particularly Alanine scanning mutagenesis on page 108, Experimental procedures: Construction of humanized version of anti-IL-8 antibody 6G4.2.5, and Tables 1 and 2).

Neither Kashmiri nor Leong teach the CDRs recited in claim 3. It is noted that claim 3 does not recite the name of the murine monoclonal antibody used in the methods of the present invention. Based on Applicant's disclosure (specification examples 1-8) it is understood that the heavy chain of SEQ ID NO: 2 and the light chain of SEQ ID NO: 4 are the heavy and light chains from the KR127 antibody.

Maeng et al. teach the murine monoclonal antibody KR127 (see the entire document, particularly pages 10-14, Figures 1 and 6). Maeng et al. do not teach the heavy and light chain sequences of the KR127 antibody, however the heavy chain of SEQ ID NO: 2 and the light chain of SEQ ID NO: 4 are inherent properties of the KR127 antibody disclosed by Maeng et al. The CDR regions recited in claim 3, the heavy chain HCDR1 (aa 31-35), HCDR2 (aa 24-34) and HCDR3 (aa 95-102) and light chain LCDR1 (aa 24-34), LCDR2 (aa 50-56) and LCDR3 (aa 89-97) are inherently present in the KR127 antibody disclosed by Maeng et al.

Thus it is the Office's position that murine monoclonal antibody comprising the heavy and light chain of SEQ ID NO: 2, SEQ ID NO: 4 of the present invention has the same structure and function as the KR127 antibody disclosed in the prior art by Maeng.

It would have been *prima facie* obvious to the person of ordinary skill in the art to humanize the KR127 antibody in order to prevent development of human anti-mouse antibodies (HAMA) in humans treated with KR127.

One would have been motivated to humanize Maeng's KR127 antibody by grafting the alanine substituted KR127 SDRs as taught by Leong and Kashmiri onto the human antibody heavy and light chain framework because Leong teaches that antibodies designed for human use should be humanized in order to prevent development of human anti-mouse antibodies (HAMA) in humans (see page 106, right paragraph).

One would have had a reasonable expectation of success to practice the present method because the methods of performing alanine scanning mutagenesis and grafting the alanine substituted CDR residues onto the human antibody framework are well established in the art as evidenced by Leong et al.

Thus the present methods would have been *prima facie* obvious to the skilled artisan at the time when the invention was made.

Claim Objection

Claims 4-10 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

No claims are allowed.

Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on June 19, 2008 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Zachariah Lucas can be reached on 571-272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Agnieszka Boesen/

Examiner, Art Unit 1648

/Stacy B Chen/

Primary Examiner, Art Unit 1648